(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 May 2002 (02.05.2002)

PCT

(10) International Publication Number
WO 02/34158 A2

(51) International Patent Classification[7]: A61F 2/00

(21) International Application Number: PCT/US01/29733

(22) International Filing Date:
21 September 2001 (21.09.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/696,349 24 October 2000 (24.10.2000) US

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(74) Agents: **JOHNSON, Philip, S.** et al.; Johnson & Johnson, One Johnson & Johnson Plaza, New Brunswick, NJ 08933 (US).

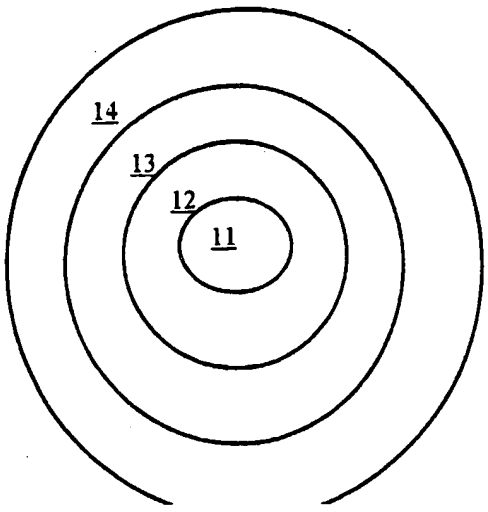
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: INTRAOCULAR LENSES AND METHODS FOR THEIR MANUFACTURE



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(57) Abstract: The present invention provides intraocular lenses that have a refractive index gradient. Additionally, the lenses of the invention may be customized to correct the ocular wavefront aberrations of a particular individual.

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INTRAOCULAR LENSES AND METHODS FOR THEIR MANUFACTURE

Field of the Invention

The present invention relates to intraocular lenses. In particular, the invention provides intraocular lenses that have a refractive index gradient. Additionally, the lenses of the invention may be customized to a particular individual.

Background of the Invention

The use of intraocular lenses to replace a patient's natural lens is well known. Generally, the intraocular lenses are formed by lathe cutting, molding, or the like. The lenses may be fixed within the eye, such as by haptics, which typically are attached in a secondary step. The lenses may be accommodating lenses that move along the optical axis of the eye to provide correction for distance and near vision. Known intraocular lenses are made of rigid materials such as polymethyl methacrylate and the like or flexible materials such as silicone, hydrogels, fluorocarbons, hydroxyethyl methacrylate, and the like.

Conventional intraocular lenses are disadvantageous in that the lenses are of a single refractive index, but are used to replace the natural lens which has a gradient refractive index. Additionally, the known intraocular lenses provide no correction for high order ocular aberrations nor are they customized to a particular individual. Therefore, a need exists for a intraocular lenses and methods for their production that overcome these disadvantages.

Brief Description of the Drawings

Fig. 1 is a magnified, cross-sectional plan view of the lens of the invention.

Description of the Invention and its Preferred Embodiments

The present invention provides intraocular lenses that incorporate one or both of a refractive index gradient and correction for ocular wavefront aberrations. The refractive index gradient provides a lens that is more similar to the natural crystalline lens than known intraocular lenses. Additionally, the lenses of the invention provide for a level of vision correction not previously available in intraocular lenses.

In one embodiment, the invention provides an intraocular lens comprising, consisting essentially of, and consisting of a refractive index gradient. The intraocular lenses of the invention may be of the type that are fixed as to centration within the eye, but move forwardly and backwardly due to ciliary muscle action. Alternatively, the lens may be an accommodating lens meaning that the lens is attached to the capsule, but is capable of changing radius and shape.

It is one discovery of the invention that by incorporating a refractive index gradient into an intraocular lens, the performance of the lens will be improved. In the lens of the invention, a refractive index gradient is provided, which gradient may be formed by use of at least two layers of materials of differing refractive indices. Generally, about 3 to about 12 layers may be used; preferably, about 4 to about 6 layers are used. In the lenses of the invention, the refractive index, from the center, or innermost layer, of the lens to its outer-most layer, may increase or decrease. Preferably, the refractive index decreases as one moves from the innermost to the outermost layers and ranges from about 1.52 to about 1.38, more preferably about 1.50 to about 1.46, most preferably about 1.44 to about 1.40. For those lenses made from rigid materials, preferably the refractive

index ranges from about 1.52 to about 1.48 from the center to the outer-most layer. For flexible materials, the range is about 1.50 to about 1.46. The change in index between the layers may be equal or unequal. Similarly, the thickness of the layers may be unequal or, preferably, equal.

The lenses of the invention may be made of any material suitable for forming intraocular lenses. For example, the lenses may be made from a rigid material including, without limitation, polymethyl methacrylate, polystyrene, polycarbonate, or the like, and combinations thereof. Additionally, flexible materials may be used including, without limitation, hydrogels, silicone materials, acrylic materials, fluorocarbon materials and the like, or combinations thereof.

For purposes of forming the inner most layer of the lens, a high refractive index monomer may be selected and polymerized or a first monomer with a first refractive index may be polymerized with a second monomer having a second refractive index in order to provide the refractive index desired. Preferably, the monomers used to form the lenses of the invention are free-radical reactive monomers.

In those lenses produced using rigid materials, the refractive index of the material may be varied by the addition of an aromatic methacrylate, halomethacrylate, or an aromatic halomethacrylate, or combinations thereof in an amount effective to increase or decrease the material to the desired level. Suitable aromatic methacrylates include, without limitation, phenyl methacrylate, naphthyl methacrylate, phenylethyl methacrylate, methoxyphenyl methacrylate, o-crsyl methacrylate, and the like, and combinations thereof. Halomethacrylates useful in the invention include, without limitation, polyfluoroalkyl methacrylates, 2-chloroethyl methacrylates, 2-bromomethacrylate, chlorocyclohexyl methacrylate, bromocyclohexylmethacrylate, and the like, or combinations thereof.

Suitable aromatic halomethacrylates include, without limitation, chlorobenzyl methacrylate, bromobenzyl methacrylate, and the like, or combinations thereof.

Similarly, these materials may be used to alter the refractive index of a flexible material such as a hydrogel or acrylic material to the desired level. In addition, chloro- or bromostyrenes may be used. For lenses made from silicone materials, the desired refractive index may be obtained by use of poly(dimethyl-co-phenylmethyl) siloxane to the material.

The materials used to form the lens may be polymerized by any known means, such as thermal, photochemical, or radiation cure using any suitable initiator including, without limitation, a thermal initiator, a UV initiator, a visible light initiator, and the like, or a combination thereof. To form the lenses of the invention, the inner-most layer may be formed by casting a rod of material of the desired refractive index and placing the rod in the center of a mold. The next lower refractive index material is dispensed into the mold and polymerized. The process may be repeated to add the desired number of layers of varying refractive index to form an intraocular lens blank. The rod then is removed from the mold, cut, and machined to form a gradient refractive index lens.

Alternatively, laminar flow mixed dosing may be used in which at least two monomers of different refractive index are dispensed with inline mixing into a mold, dispensing the low index material prior to the high index material. The flow rate is adjusted so that no mixing occurs in the mold. The dispensed material then is cured to produce a linear gradient index lens.

The conditions under which the materials are cured will depend on the method selected to produce the lens and the materials being used to form the lens. It

is within the skill of one of ordinary skill in the art to determine the precise cure conditions.

In forming the lens, the flexibility of the material becomes more critical as one moves from the inner-most layer to the outermost layer, the outermost layers being the more flexible. This may be controlled by a number of factors including, without limitation, the glass transition temperature, modulus, and water content of the material. In formation of the layers making up the lens, the compatibility of one layer with another to be added to it may be increased by treatment, such as by plasma treatment, prior to addition of the next layer.

The lenses of the invention may be anchored within the lens capsule by any known means such as the use of haptics. Additionally, a photoreactive tissue cement may be used including, without limitation, fibrin, cyanoacrylate, photo-curable gelatin, and the like, or combinations thereof. Means for anchoring the lenses within the eye for both fixed and accommodating lenses are well known. The lenses of the invention may be implanted in any region into which intraocular lenses are typically implanted such as the anterior or posterior chamber, or any of a variety of positions in or on the cornea.

In Fig. 1 is depicted lens 10 of the invention. Lens 10 has innermost layer 11 having a refractive index of 1.50. Layer 12 overlays layer 11 and is of a refractive index of 1.49. Similarly, layers 13 and 14 overlay layers 12 and 13, respectively, each having a refractive index of 1.48 and 1.47, respectively.

In another embodiment, the invention provides an intraocular lens for an individual comprising, consisting essentially of, and consisting of an anterior and a posterior surface, wherein one or both of the surfaces is suitable to substantially correct one or more wavefront aberrations of the individual. In yet another

embodiment, the invention provides an intraocular lens for an individual comprising, consisting essentially of, and consisting of a refractive index gradient, an anterior surface, and a posterior surface, wherein one or both of the surfaces is suitable to substantially correct one or more ocular wavefront aberrations of the individual.

Ocular wavefront aberrations, generally, are wavefront aberrations of the eye that are departures from a spherical wavefront at any position on the wavefront. The classic description of these aberrations are spherical aberration, astigmatism, coma, and distortion.

Alternatively, the aberrations may be mathematically described, for example using Zernike polynomials. Apparatuses for performing the aberration measurements include, without limitation, aberroscopes, devices that measure ocular Modulation Transfer Function by point spread or line spread, or any similar devices that measure, estimate, interpolate, or calculate the ocular optical wavefront . A suitable aberroscope for carrying out the measurements is available from Wavefront Sciences, Inc, Albuquerque, New Mexico. Preferably, the intraocular lenses of the invention correct high order ocular wavefront aberrations.

The lenses of the invention may be designed to provide multifocal correction. For example, in the case of the designing of an accommodating intraocular lens, the wavefront measurement of the eye may be carried out by providing the lens wearer visual targets at at least two different distances, a first and a second distance. For example, one target may be provided in the lens wearer's distance vision zone, the target being about 15 feet or more from the eye. A second target may be provided in the near vision zone, the target being about 30 to about 50 cm from the eye. Preferably, a target also is provided in the lens wearer's intermediate vision zone, the target being about 50 to about 80 cm from the wearer's eye. It is known in the art how to utilize available devices available for aberration measurement at far, near and intermediate distances.

After the aberration measurements are obtained, the measurements are mathematically converted to a height difference thus providing an elevation map above and below a designated mean sphere value, known as the optical path difference. Correction for the aberrations will be provided by introduction of an optical path difference, or aberration inverse filter, that offsets the distortions due to the ocular aberrations.

The converted differences are used to provide the desired lens. The data may be transformed onto a grid pattern of a rectilinear, polar concentric, or spiral format to correspond to the mechanism by which the surface of the lens, or a mold used to form the lens, may be tooled using a computer numeric controlled ("CNC") lathe. The required changes in the lens' surface elevation or slope to achieve correction of the aberrations may be incorporated onto the lens' front surface, back surface, or a combination thereof.

In the cases in which the lenses of the invention are multifocal, one or both of the front, or convex, surface and back, or concave, surface of the lens may contain an optic zone that corrects the lens wearer's ocular wavefront aberrations for distance, near, and optionally intermediate vision. In an alternative embodiment, aberration correction may be divided between the front and back surfaces.

In addition to wavefront aberration compensating surfaces, one or more surfaces of the intraocular lens may be of a geometry that substantially corresponds with that of the lens wearer's cornea. The corneal topographic data for the lens wearer may be acquired using conventional topographers.

What is claimed is:

1. An intraocular lens comprising, a refractive index gradient.

2. The intraocular lens of claim 1, further comprising at least two layers of materials of differing refractive indices.

3. The intraocular lens of claim 2, further comprising about 3 to about 12 layers of materials of differing refractive indices.

4. The intraocular lens of claim 2, wherein, from the innermost layer of the lens to its outermost layer, the refractive indices of the layers range from about 1.52 to about 1.38.

5. An intraocular lens for an individual comprising an anterior and a posterior surface, wherein one or both of the surfaces is suitable to substantially correct one or more ocular wavefront aberrations of the individual.

6. The intraocular lens of claim 5, further comprising a refractive index gradient.

7. The intraocular lens of claim 6, further at least two layers of materials of differing refractive indices.

8. The intraocular lens of claim 7, further comprising about 3 to about 12 layers of materials of differing refractive indices.

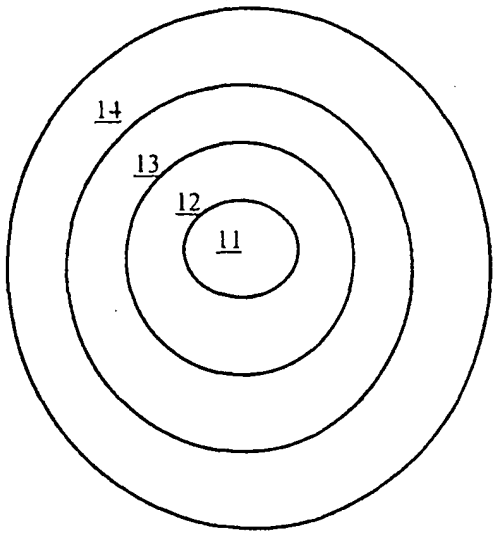
9. The intraocular lens of claim 7, wherein, from the innermost layer of the lens to its outermost layer, the refractive indices of the layers range from about 1.52 to about 1.38.

10. The intraocular lens of claim 5, further comprising one or more surfaces of a geometry that substantially corresponds to the individual's corneal topography.

11. The intraocular lens of claim 6, further comprising one or more surfaces of a geometry that substantially corresponds to the individual's corneal topography.

12. The intraocular lens of claim 7, further comprising one or more surfaces of a geometry that substantially corresponds to the individual's corneal topography.

FIG. 1



(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 May 2002 (02.05.2002)

PCT

(10) International Publication Number
WO 02/034158 A3

(51) International Patent Classification[7]: A61F 2/16

(21) International Application Number: PCT/US01/29733

(22) International Filing Date:
21 September 2001 (21.09.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/696,349 24 October 2000 (24.10.2000) US

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(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
12 December 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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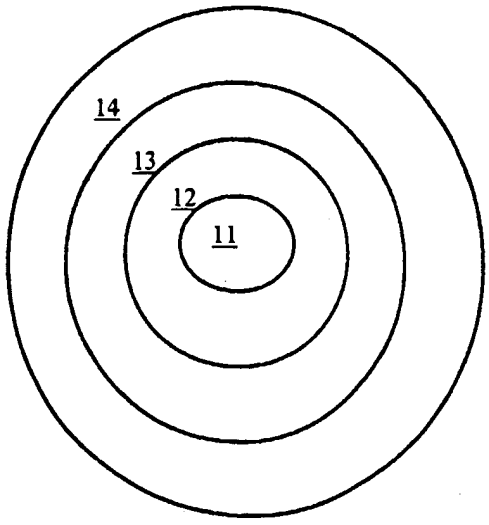

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WO 02/034158 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/29733

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F2/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

	Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
2	X	WO 92 10980 A (EASTMAN KODAK CO) 9 July 1992 (1992-07-09)	1-3
	A	page 9, line 1 - line 17; figures 2,4 page 11, line 13 - line 32; figure 8	4

2	X	FR 2 655 842 A (MAIGRET YVES;BAIKOFF GEORGES) 21 June 1991 (1991-06-21) page 2, line 10 -page 3, line 31; figure 1	1-3

2	X	US 5 877 839 A (PORTNEY VALDEMAR) 2 March 1999 (1999-03-02) column 6, line 38 -column 7, line 14; figure 7	1-3

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 March 2002	08. 07. 2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	WOLF C.

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INTERNATIONAL SEARCH REPORT

ernational application No.
PCT/US 01/29733

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-4

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-4

an IOL comprising a refractive index gradient

2. Claims: 5-12

an IOL for an individual comprising an anterior and a posterior surface,wherein one or both of the surfaces is suitable to substantially correct one or more ocular wavefront aberrations of the individual.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 01/29733

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